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Socioeconomic and Racial Disparities in the Selection of Chest-Wall Boost Radiation in California Women Following Mastectomy

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Abstract

Introduction—Health care disparities are well documented in breast cancer. We investigated socioeconomic (SES) and racial factors in women with locally-advanced breast cancer from the California Cancer Registry receiving post-mastectomy radiation therapy (PMRT) with or without a chest-wall boost (CWB).

Patients and Methods—Records of 4,747 women with invasive breast cancer, diagnosed from 2005-2009, treated with PMRT were reviewed and stratified based on treatment with (n=2,686 [57%]) or without (n=2,061 [43%]) a CWB. Various patient demographic and biologic factors were analyzed using univariate and multivariate analysis.

Results—Reception of a CWB was associated with race/ethnicity ($p<0.001$) and SES ($p<0.001$) on univariate analysis, along with tumor size ($p=0.038$), tumor grade ($p=0.033$), Her-2 status ($p=0.015$), AJCC stage ($p=0.001$), number of nodes examined ($p=0.001$), and number of nodes positive ($p=0.037$). Controlling for confounding factors, race/ethnicity and SES remained independently predictive of a CWB. Hispanic women were more likely to receive a CWB compared to Asian (HR 0.74, CI 0.60-0.90), Black (HR 0.63 CI 0.48-0.83), or White (HR 0.81, CI 0.69-0.95) women, and women of low SES were more likely to receive a CWB compared to women of high SES (HR 0.74, CI 0.64-0.86).

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CONFLICTS OF INTEREST: None for all authors.

Conclusion—We identified that poor and Hispanic women were more commonly treated with a CWB compared to more affluent and non-Hispanic women of similar stage, biology, and treatment paradigm.

Keywords

Post-Mastectomy Radiation Therapy; Breast Cancer; Chest Wall Boost; Health Care Disparities; Minority Populations; Hispanic Ethnicity; Socioeconomic Status

INTRODUCTION

Racial disparities have been well documented in breast cancer. Compared to White women, lower incidence and higher mortality rates have been demonstrated in non-Hispanic Black women, while Hispanic women have been shown to have both lower incidence and lower mortality rates.[1,2] The rate of breast conservation surgery vs. mastectomy in appropriately staged women and the rate of systemic therapy reception are also lower in Black and Hispanic women compared to White women.[3-7]

Socioeconomic (SES) disparities and limited access to care may significantly confound racial differences in biology or natural history of breast cancer.[8-10] Census tracts with higher poverty status are more likely to display significant differences in breast cancer mortality in both Black and Hispanic women.[11] A national cohort study of breast cancer patients found that uninsured women, Medicaid enrollees, and younger Medicare beneficiaries were less likely to receive definitive locoregional therapy and adjuvant systemic treatments compared to privately insured women.[12]

Prospective randomized trials have demonstrated that post-mastectomy radiation therapy (PMRT) improves breast cancer survival (BCS) and overall survival (OS), and that the area at the highest risk for local recurrence is the chest wall (5% to 15%).[13-18] Risk factors that may contribute to this local failure include young age, lympho-vascular invasion (LVSI), triple negative status, poor response to neo-adjuvant chemotherapy, inflammatory presentation, large tumor size, hormone receptor status, number of positive nodes (≥4), and positive margins.[18,19] Landmark trials did not treat women with focal dose escalation to the mastectomy scar, known as a chest wall boost (CWB), and there are no additional prospective data on the benefit of a CWB or specifications regarding when it should be utilized.[19-21] Furthermore, CWB has shown to increase skin toxicity that led to early cessation of the treatment course.[22] Resulting controversy and practice pattern variability exist in the utilization of a radiation boost to the chest wall (CWB). Some centers have reported consistent use of a CWB with PMRT,[23,24] and improved local recurrence rates.[24]

The purpose of the present study was to evaluate, using a population-based cohort from the California Cancer Registry (CCR), the influence of race and SES in the selection of a chest-wall boost (CWB) following post-mastectomy radiation therapy (PMRT) for breast cancer.

PATIENTS AND METHODS

Data

A retrospective observational study of first-primary, invasive breast cancer cases diagnosed from 2005-2009, treated with mastectomy followed by PMRT, was conducted utilizing the California Cancer Registry (CCR). This statewide population-based data is comprised of three registries (Greater Bay Area, Los Angeles, and Greater California) that are part of the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program; the data has had standardized collection and quality control protocols since 1988. The CCR has demographic and tumor information obtained from medical records. Data available include age and marital status at diagnosis, race/ethnicity, tumor size, presence of lymph node involvement, cancer stage according to the American Joint Committee on Cancer (AJCC), tumor grade, histology, laterality, focality; expression of estrogen receptor (ER), progesterone receptor (PR) and Her2/neu (HER2); other cancer treatments including surgery and radiation, and vital status at the time of last contact or vital status record linkage.

Patients

Records of women with invasive breast cancer were reviewed and stratified based on whether a CWB was received or not following PMRT. Race and ethnicity groups were defined as non-Hispanic White (NHW), non-Hispanic Black (NHB), non-Hispanic Asian/Pacific-Islander (API), and Hispanic (HSP). Race and Hispanic ethnicity was based on abstraction from medical records, and Hispanic ethnicity was further enhanced by the North American Association of Central Cancer Registries Hispanic Identification Algorithm (NHIA).[25] We did not further classify Hispanics by country of origin. Low, medium, and high SES were defined by a well-utilized and previously-described[26] method of geographic area-based composite SES measure using specific variable quintiles from the 2000 U.S. census.

Analysis

Race/ethnicity and SES between the cohorts were analyzed using the χ^2 test of independence to compare differences in individual- and clinical-level variables between patients who received CWB versus those who did not. Adjusting for potential confounders, multivariate logistic regression models were used to identify predictors of CWB reception, reported as odds ratios (OR) with 95% confidence intervals (CI); significance was set at $p < 0.05$ and all tests were two-sided. Geographic distribution of CWB reception versus no CWB reception was assessed by California hospital referral region (HRR)[27] and compared to geographic distribution of Hispanic ethnicity and poverty by California county using a Pearson correlation coefficient matrix.[28]

RESULTS

Overall, our cohort consisted of 4,747 women who received PMRT. The majority of women (32%) were at least age 60, while 29% and 26% were in their 40's and 50's. Fifty-six percent were stage III, 35% stage 2, and 5% stage 1, with 53% of patients having 2 to 5 cm tumors and 49% being grade 3 or 4. Estrogen receptor positivity was confirmed in 65%,

along with 61% progesterone receptor positivity, while only 26% were Her-2 positive (overall 60% luminal A tumors) (Table 1). Median follow-up was 43.6 months. Fifty-seven percent (n=2,686) received a chest wall boost, while 43% (2,061) did not. Participants were NHW (59%), NHB (6%), API (15%), HSP (21%), and of high (51%), middle (20%), or low (29%) SES (Table 1). The distribution of race among high vs. low SES patients was, respectively, NHW (69% vs. 40%), NHB (3% vs. 11%), API (17% vs.11%), and HSP (11% vs. 38%). The distribution of SES among NHW, NHB, API, and HSP race/ethnicity was high (60%, 26%, 59%, 26%), middle (20%, 18%, 20%, 21%), and low (19%, 56%, 21%, 53%). Fifty-four percent, 58%, and 58% of NHW women of high, medium, and low SES, respectively, received a CWB compared to 55%, 58%, and 69% of all HSP women (Figure 1).

Univariate analysis revealed that CWB reception was associated with race/ethnicity ($p<0.001$), SES ($p<0.001$), tumor size ($p=0.038$), tumor grade ($p=0.033$), Her-2 status ($p=0.015$), AJCC stage ($p=0.001$), number of nodes examined ($p=0.001$), and number of nodes positive ($p=0.037$) (Table 2). There were no significant differences between those who received a CWB and those who did not with respect to age, urbanization level, laterality, ER/PR status, tumor subtype, chemotherapy reception, or hormone therapy reception.

On multivariate analysis, HSP ethnicity (vs. NHW, NHB, API, $p=0.01$, 0.001, and 0.003, respectively) and low-SES status (vs. high, $p<0.001$) retained strong significant association with CWB reception while controlling for stage, grade, positive nodes, number of nodes examined, and HER-2 status (Table 3). Other factors also independently predicting reception of a CWB on multivariate analysis were stage III disease (vs. 2, $p=0.028$), and 10 or more nodes examined (vs. less than 10, $p=0.035$). There was substantial geographic heterogeneity of CWB prescription between HRR (Table 4), which did not correlate to ethnicity (correlation coefficient $r=0.36$, $p=0.08$) or poverty ($r=0.16$, $p=0.44$).

DISCUSSION

This large observational retrospective study of California women with locally-advanced breast cancer treated with mastectomy and PMRT reports that low SES and Hispanic ethnicity are independently predictive of reception of a CWB. We hereafter explore potential confounding factors that may contribute to this disparity.

Clinical and pathological factors that may influence a treating physician to deliver a chest wall boost include positive mastectomy margin, lympho-vascular space invasion (LVSI), prior regional failure, triple-negative tumor marker status, poor response to neoadjuvant chemotherapy, T4 disease, age less than 45, large tumor size, hormone receptor status, number of positive nodes (≥4), and inflammatory breast cancer.[24,29-36] Our multivariate analysis also identified number of nodes examined (≥10) and stage III as independent predictors of a CWB. Practice patterns and limited access to alternate medical care may also be influential, if, for example, providers practicing in predominantly Hispanic or low SES geographic regions maintain any historical CWB-favoring prescription precedence of institutions at which they trained. We could not explore the influence of margin status,

lympho-vascular invasion on the receipt of a CWB due to the limitation of the CCR database.

Hispanic ethnicity and low SES remained independently predictive of a CWB in our multivariate logistic regression analysis, which controlled for all of the aforementioned confounders except LVSI and positive margins. These latter two parameters were not collected within the CCR for the diagnosis years of our cohort. Although we cannot control for this potential confounding influence we note that all other discoverable risk factors for LRR cumulatively did not negate the association between race/ethnicity and SES to the reception of a CWB, which were the strongest of all associations (Table 3).

The correlation between geographic distribution of physician CWB prescription patterns and ethnic and socioeconomic density was also considered to be a potential confounder of our findings. This was evaluated by stratifying patients treated with and without a CWB by California HRR in relation to United States Census Bureau statistics of Hispanic population and poverty level density by county of residence. We found significant variation of CWB delivery geographically, but that this did not correlate with the geographic distribution of Hispanic ethnicity or impoverishment (Table 4). While a percentage of patients may have traveled outside of their county of residence for treatment, the comparison provides a crude assessment that the heterogeneity of prescription pattern by location does not closely mimic that of SES or ethnicity. It is, therefore, less likely that the increased rates of CWB observed in poor and Hispanic women can be explained by geographic variability of practice patterns or proximity of poor and Hispanic women to providers who routinely prescribe a CWB for all cases of PMRT.

Physician bias towards Hispanic and poor women may also have contributed to increased rates of CWB reception. We have anecdotally observed a propensity of physicians to prescribe alternative treatments to patients perceived as incapable of compliant follow-up. We coin the term “likely-lost effect” to define this phenomenon. Women of Hispanic ethnicity and low SES may have more commonly been prescribed a CWB in order to maximize theoretical benefit of escalated treatment aimed to prevent missed opportunities for early salvage treatment of recurrent disease if patients are noncompliant to follow-up.

The likely-lost effect may bias provider decision making in other scenarios more likely to affect oncologic outcomes and quality of life than the decision of CWB prescription. For example, a patient may be denied a time-intensive definitive radiation regimen in favor of a shorter palliative regimen, be treated with less intense chemotherapy requiring fewer laboratory studies or conveying less risk, or be offered early treatment as opposed to an equally-appropriate watch-and-wait strategy if deemed unlikely to comply with close follow up. Awareness of this potential bias may encourage providers to optimize support services to address barriers to compliant follow-up and discourage hasty racial or economic profiling of patients. Discrepant lengths of follow-up between the boost and no-boost cohorts and by race/ethnicity and SES status were hypothesized but un-assessable. The CCR uses a passive follow-up mechanism to gauge survival that is independent of provider, often utilizing death certificates and other publically-available administrative databases. It does not collect length of patient-with-provider follow-up.

However, an association between race/ethnicity or SES and follow-up compliance has not been definitively demonstrated in prospective studies. Small retrospective studies[3,37,38] have reported conflicting results that race/ethnicity may have no association with kept appointments.[39] A number of other barriers to compliant follow up, such as finance, transportation, distress management, social support, language barriers, etc. may influence compliant follow up[40] and should be simultaneously considered prior to treatment escalation, as well as the increased risk of acute and late toxicity. [22]

A major strength of our study is its population base – breast cancer cases from the entire state of California. The CCR has been a statewide database since 1988 and is one of the largest cancer registries in the world. The registry is also part of the SEER program through contracts to three Regional Registries within the state of California, and meets all of the quality and completeness standards of the National Cancer Institute SEER program as well as those of the National Association of Central Cancer Registries. The study has a large number of patients (n=4,747), providing statistical power for most of the analyses. The major limitation is the lack of data regarding margin status and LVS.

CONCLUSIONS

Poor women of any race and Hispanic women were more commonly treated with a CWB compared to more affluent and non-Hispanic women of similar stage, biology, and treatment paradigm. Our investigation reveals a previously unreported provider bias to treat poor and Hispanic women with more escalated treatment. Variation in geographic prescription patterns and the “likely-lost effect” may potentially contribute to this disparity.

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CLINICAL PRACTICE POINTS

- The utilization of a chest wall boost (CWB) following post-mastectomy radiation therapy (PMRT) remains controversial.
- Socioeconomic and racial disparities exist in the natural progression of breast cancer, disease-specific mortality and the type of therapy received.
- A population-based examination of the prescription practices found that low SES and Hispanic ethnicity were independently predictive of a receipt of CWB.
- The likely-lost effect may be a bias in provider decision-making that partially accounts for the prescription differences.

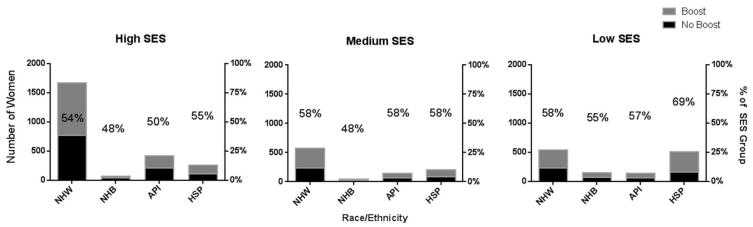

Figure 1.
Percentage of Women of Each SES Receiving CWB by Race/Ethnicity

Table 1

Patient and Tumor Characteristics

	Overall, N=4,747	
Characteristic	**#**	**(%)**
Age		
<40 years	592	12%
40-49 years	1387	29%
50-59 years	1256	26%
60+ years	1512	32%
Race/Ethnicity		
non-Hispanic white	2789	59%
non-Hispanic black	276	6%
Hispanic	975	21%
non-Hispanic Asian/PI	707	15%
SES *		
Low	1359	29%
Medium	968	20%
High	2420	51%
Tumor Size		
<2cm	800	17%
2-5cm	2509	53%
>5cm	1438	30%
Grade		
1	479	10%
2	1938	41%
3/4	2330	49%
ER Status		
Positive	3535	75%
Negative	1212	26%
PR Status		
Positive	2915	61%
Negative	1832	39%
Her2 Status		
Positive	1238	26%
Negative	3509	74%
Subtypes		
Luminal A/B	2832	60%
Luminal-her2	753	16%
Triple Negative	677	14%

	Overall, N=4,747	
Characteristic	**#**	**(%)**
Her2 enriched	485	10%
AJCC Stage		
I	258	5%
II	1655	35%
III	2639	56%
IV	195	4%
Nodes Examined		
<10 nodes examined	1493	31%
10 or more nodes examined	3254	69%
Nodes Positive/Negative		
All Nodes Negative	923	19%
Positive Nodes Present	3824	81%
Chemotherapy		
No	701	15%
Yes	4046	85%
Hormone Therapy		
No	2300	48%
Yes	2447	52%

* Low SES = quintiles 1,2; Mid SES = quintile 3; High SES = quintiles 4,5.

Table 2

Patient Demographics: Radiation Chest-Wall Boost v. No Chest-Wall Boost Univariate Analysis.

	No Boost, N=2,061 (43%)		Boost, N=2,686 (57%)		
Characteristic	**#**	**(%)**	**#**	**(%)**	***P-Value*** [#]
Age					0.095
<40 years	265	45%	327	55%	
40-49 years	636	46%	751	54%	
50-59 years	526	42%	730	58%	
60+ years	634	42%	878	58%	
Median (range)	52 (23-93)		53 (20-92)		
Race/Ethnicity					**<.001**
non-Hispanic white	1241	45%	1548	56%	
non-Hispanic black	132	48%	144	52%	
Hispanic	358	37%	617	63%	
non-Hispanic Asian/PI	330	47%	377	53%	
SES [*]					**<.001**
Low	518	38%	841	62%	
Medium	411	42%	557	58%	
High	1132	47%	1288	53%	
Tumor Size					**0.038**
<2cm	380	48%	420	53%	
2-5cm	1071	43%	1438	57%	
>5cm	610	42%%	828	58%	
Grade					**0.033**
1	224	47%	255	53%	
2	868	45%	1070	55%	
3/4	969	42%	1361	58%	
ER Status					0.221
Positive	1553	44%	1982	56%	
Negative	508	42%	704	58%	
PR Status					0.295
Positive	1283	44%	1632	56%	
Negative	778	42%	1054	58%	
Her2 Status					**0.015**
Positive	501	40%	737	60%	
Negative	1560	44%	1949	55%	
Subtypes					0.083
Luminal A/B	1257	44%	1575	56%	
Luminal-her2	312	41%	441	59%	

	No Boost, N=2,061 (43%)		Boost, N=2,686 (57%)		
Characteristic	**#**	**(%)**	**#**	**(%)**	***P-Value*** [#]
Triple Negative	303	45%	374	55%	
Her2 enriched	189	40%	296	61%	
AJCC Stage					**0.001**
I	112	43%	146	57%	
II	775	47%	880	53%	
III	1081	41%	1558	59%	
IV	93	47%	102	52%	
Nodes Examined					**0.001**
<10 nodes examined	701	47%	792	53%	
10 or more nodes examined	1360	42%	1894	58%	
Nodes Positive/Negative					**0.037**
All Nodes Negative	429	46%	494	54%	
Positive Nodes Present	1632	43%	2192	57%	
Chemotherapy					0.380
No	315	45%	386	55%	
Yes	1746	42%	2300	57%	
Hormone Therapy					0.542
No	1009	44%	1291	56%	
Yes	1052	42%	1395	57%	

[*] Low SES = quintiles 1,2; Mid SES = quintile 3; High SES = quintiles 4,5. Some number may not sum to 100 due to rounding.

[#] Univariate analysis.

Table 3

Multivariate Logistic Regression Identifying Predictors of Receiving Chest Wall Boost.

Independent Variables (Referent)	Odds Ratio	95% CI		P-Value
		Lower	Upper	
Race/Ethnicity (Hispanic)				
Non-Hispanic White	0.81	0.69	0.95	**0.010**
Non-Hispanic Black	0.63	0.48	0.83	**0.001**
Non-Hispanic Asian/PI	0.74	0.60	0.90	**0.003**
AJCC Stage (III)				
I	1.15	0.84	1.59	0.384
II	0.86	0.75	0.98	**0.028**
IV	0.77	0.57	1.03	0.076
SES (Low)*				
Middle	0.86	0.72	1.02	0.075
High	0.74	0.64	0.86	**<0.001**
Tumor Grade (3/4)				
1	0.87	0.71	1.07	0.180
2	0.92	0.81	1.04	0.199
Nodes Status (All Negative)				
Positive Nodes Present	1.08	0.89	1.29	0.443
Her2 Status (Positive)				
Negative	0.88	0.77	1.01	0.071
Nodes Examined (≥10 nodes examined)				
<10 nodes examined	0.86	0.75	0.99	0.035

* Low SES = quintiles 1, 2; Mid SES = quintile 3; High SES = quintiles 4, 5

Table 4

CWB vs. no CWB and percent Hispanic and impoverished by California Hospital Referral Region (HRR) or county

HRR (County, if different)	CWB/no-CWB	Hispanic (2010)	Poverty (2012, all ages)
Bakersfield (Kern)	3.8	49%	24%
Redding (Shasta)	2.8	8.4%	17%
Santa Barbara	2.6	43%	16%
Salinas (Monterey)	2.5	55%	18%
Orange County	2.3	34%	13%
Napa	2.2	32%	9.7%
San Diego	1.9	32%	15%
Ventura	1.9	40%	12%
Los Angeles	1.6	48%	19%
Palm Springs/Rancho Mirage (Riverside)	1.4	46%	18%
San Bernardino	1.4	49%	20%
Alameda County	1.1	23%	13%
Sacramento	1.0	22%	20%
Santa Rosa	1.0	25%	12%
Fresno	0.98	50%	28%
San Mateo	0.76	25%	8.4%
San Francisco	0.74	15%	15%
Contra Costa	0.74	24%	11%
Stockton (San Joaquin)	0.72	39%	19%
Modesto (Stanislaus)	0.69	42%	20%
Santa Cruz	0.68	32%	14%
Chico	0.60	14%	22%
San Jose (Santa Clara)	0.51	27%	11%
San Luis Obispo	0.50	21%	14%
Mean	1.30	33%	16%

HRR- Hospital Referral Region CWB/no-CWB ratio defined by CCR using HRR as defined by the Dartmouth Atlas of Health Care (www.dartmouthatlas.org). Hispanic and poverty percentages from US Census data by county (www.census.gov).